REMARKS

I. Introductory Remarks

Applicants respectfully request reconsideration of this application in view of the foregoing amendments and following remarks.

Upon entry of the foregoing amendments, claims 21-25, 29 and 31 will remain pending in this application. Claims 21-23 are being amended. Claim 30 is being cancelled. No claims are being added.

Exemplary support for the claim amendments exists in the specification at page 5, lines 11-17; page 17, line 26 through page 18, line 4; page 49, lines 5-8; page 74, lines 18-23; and original claim 22.

II. Response to the Restriction Requirement

In a telephone conversation with Beth Burrous on November 5, 2003, the Examiner restricted the invention into the following groups:

1. Claims 17-18, drawn to antibodies that specifically bind AUR1 and AUR2 polypeptide and hybridomas that product the antibodies,
2. Claims 21-25 and 29-31, drawn to methods of treating a disease in a patient utilizing modulators of AUR1 and AUR2 polypeptides, and
3. Claim 28, drawn to antisense oligonucleotides.

Applicants hereby confirm their election, without traverse, of Group 2 for prosecution in this application. The election originally was communicated to Examiner Monshipouri by telephone on November 7, 2003.

III. Claims 24 and 31 Comply with 35 U.S.C. § 112, Second Paragraph

Claims 24 and 31 were rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the invention. More particularly, the Office questioned how antisense *nucleic acids* can modulate Aurora *protein* activity. Applicants respectfully traverse the rejection.

The Office has viewed the term "modulates" too narrowly. The specification states that "'modulates' refers to the ability of a compound to alter the function of AUR1 and/or AUR2" and "refers to altering the function of AUR1 and/or AUR2 by increasing or decreasing the probability that a complex forms between AUR1 and/or AUR2 and a natural binding partner." Page 16, lines 14-15 and 22-24. These definitions do not require direct interaction of a modulator with an Aurora polypeptide.

Antisense nucleic acids *indirectly* modulate Aurora protein activity by reducing the amount of Aurora protein in cells. The amount of a protein impacts the protein's function in a cell. Likewise, the amount of a protein clearly affects whether a complex forms between the protein and its binding partner.

For these reasons, claims 24 and 31 are not indefinite, and Applicants request withdrawal of the rejection.

IV. Claims 21-25 and 29-31 Comply with the Enablement Requirement of 35 U.S.C. § 112, First Paragraph

Claims 21-25 and 29-31 were rejected as allegedly failing to comply with the enablement requirement of 35 U.S.C. § 112, first paragraph. The Office based this rejection on four assertions: (1) the structural definition of Aurora polypeptides is too broad, (2) diseases suitable for treatment are not identified, (3) the specification contains no working examples of the claimed methods, and (4) the nature of Aurora activity is not specified. Applicants respectfully disagree.

As amended, the claims relate to modulating the activity of a *full length* AUR-1 or AUR-2 protein. The recitation of full length proteins obviates the Examiner's concern about small Aurora polypeptides. Applicants, however, do not acquiesce to the propriety of the Office's rejection, and have amended the claims solely to advance prosecution.

The amended claims also recite diseases suitable for treatment with Aurora modulators. The inventors have established a clear link between Aurora proteins and these diseases. Example 2 of the specification demonstrates that AUR-1 mRNA is highly expressed in human colon, lung, breast, melanoma and renal cancer cell lines, but not in

normal adult human tissues other than thymus tissue. Example 2 also shows that AUR-2 is highly expressed in colon cancer cell lines and moderately expressed in lung cancer cell lines. Example 7 further demonstrates that AUR-1 and AUR-2 are expressed in 96% of colon, renal, melanoma and breast human tumor cell lines. Accordingly, the application and claims clearly specify diseases suitable for treatment with Aurora protein modulators.

Contrary to the Office's suggestion, the specification also contains working examples that support the pending claims. Examples 10 and 11 show that Aurora proteins contribute to the malignant phenotype. In Example 10, rat fibroblasts expressing wild-type AUR-2 formed colonies in soft agar, whereas rat fibroblasts expressing a kinase inactive AUR-2 did not do so. Example 11 further demonstrates that AUR-2 confers a growth advantage to NIH3T3 cells in low serum and anchorage-independent growth. Example 12 shows that modulators of Aurora proteins inhibit the growth of tumor cells. In that example, antisense molecules down-regulated AUR-2 protein expression in the human tumor cell line H1299 to an undetectable level. The down-regulation inhibited growth of the tumor cell line and appeared to induce apoptosis, as measured by fluorescence activated cell sorting. These examples constitute strong evidence that one skilled in the art could practice the claimed methods of treating human cancer by administering an Aurora modulator to an afflicted patient.

Finally, the amended claims particularly relate to the modulation of Aurora *kinase* activity. Thus, the Office's concern that the claims do not specify a particular Aurora activity is moot. Pages 49-52 of the specification provide many examples of compounds that modulate kinase activity, and the specification also describes methods of screening for additional modulators.

For these reasons, claims 21-25 and 29-31 are enabled by the application's disclosure, and Applicants request withdrawal of the rejection.

V. Claims 21-25 and 29-31 Comply with the Written Description Requirement of 35 U.S.C. § 112, First Paragraph

Claims 21-25 and 29-31 were rejected as allegedly failing to comply with the written description requirement of 35 U.S.C. § 112, first paragraph. More particularly, the Office stated that the genus of Aurora polypeptides and the genus of Aurora modulators are not

adequately described. Regarding the genus of polypeptides, the Office stated that the claims embrace "many functionally unrelated fragments." Regarding the genus of modulators, the Office stated that the claims embrace a large genus with "potentiality of retaining many activities," and that the "specification discloses only a single species . . . , namely kinase modulators."

In view of the amendments set forth and discussed above, this rejection is moot. The claims now relate to modulating the *kinase* activity of a *full length* AUR-1 or AUR-2 protein. Accordingly, Applicants request withdrawal of the rejection.

VI. Concluding Remarks

Applicants believe that the application is now in condition for allowance, and request favorable reconsideration of it.

If the Examiner believes that a telephone interview will advance prosecution of the application, she is invited to contact the undersigned by telephone.

The Commissioner is hereby authorized to charge any additional fees that may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of

papers submitted herewith, Applicants hereby petition for such extension under 37 C.F.R. § 1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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